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Primary Benzylamines by Efficient N-Alkylation of Benzyl Alcohols Using Commercial Ni Catalysts and Easy-to-Handle Ammonia Sources

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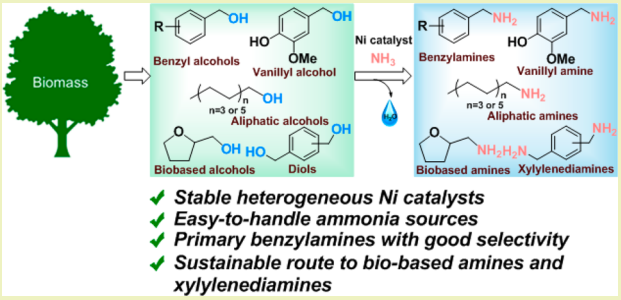
Supporting Information

ABSTRACT: Primary benzylamines are highly important building blocks in the pharmaceutical and polymer industry. An attractive catalytic approach to access these compounds is the direct coupling of benzyl alcohols with ammonia via the borrowing hydrogen methodology. However, this approach is usually hampered by a series of side-reactions, one of the most prominent being the overalkylation of the formed primary amine. Herein, we describe a robust catalytic methodology, which utilizes commercially available heterogeneous Ni catalysts and easy-to-handle ammonia sources, such as aqueous ammonia or ammonium salts, for the formation of primary benzylamines with good selectivity and scope. Notably, our method enables the conversion of potentially lignin-derived vanillyl alcohol to vanillylamine, which can be used to produce emerging biobased polymers or as pharma building blocks. Important sugar derived platform alcohols as well as long chain aliphatic primary alcohols can be successfully aminated. Moreover, we provide an alternative, sustainable route to *p*-xylylenediamine and *m*-xylylenediamine, important components of heat resistant polyamides such as Kevlar.



KEYWORDS: *Aqueous ammonia, Vanillyl alcohol, Biobased amines, Vanillylamine, Nickel catalysis*

INTRODUCTION

Primary benzylamines are crucially important building blocks in the chemical industry. They are omnipresent moieties in biologically active compounds[1,2] and prominent scaffolds in widely used polymers,[3,4] thus the development of sustainable pathways to gain access to these compounds from readily available, inexpensive starting materials is of high importance. Especially primary benzylamines are important building blocks for further derivatization in the pharmaceutical or polymer industry.[3] Generally, these are obtained through the reaction of benzyl chloride with NH_3, a process that generates stoichiometric amounts of chloride salts as byproducts.[5,6]

A highly attractive and more environmentally friendly approach to generate the desired benzylamines would be to couple benzyl alcohols with the inexpensive and widely available ammonia, directly. This can be accomplished through the borrowing hydrogen methodology, which is atom-economic and waste-free and requires careful design or selection of an appropriate catalyst system capable to transfer hydrogen equivalents from the alcohol substrates to the corresponding imine intermediate to form the desired amine product.[7−12]

Surprisingly, despite their clear importance, only a few reports addressed the formation of primary benzylamines by the direct coupling of ammonia with benzyl alcohols using homogeneous[13−15] or heterogeneous[14−17] catalytic systems. This could be attributed to the fact that obtaining primary benzylamines in high selectivity has proven to be very challenging due to side reactions such as overalkylation of the formed primary amine product.[7,8]

The pioneering works of Shimizu have described a few examples of primary benzylamine synthesis from alcohols and ammonia gas, employing Ni/Al_2O_3 and $CaSiO_3$ as catalysts.[16,17] Shi reported the catalytic activity of $NiCuFeO_x$ adopted for the alkylation of NH_3.[18] More recently, Hii obtained primary benzylamines using commercially available $Ni/Al_2O_3{-}SiO_2$ and ammonia gas in a continuous flow setup.[19] On the basis of these excellent works, we aimed at the development of new catalyst systems for the amination of important and not yet addressed substrates, primarily those that could be derived from various renewable resources. Thus,

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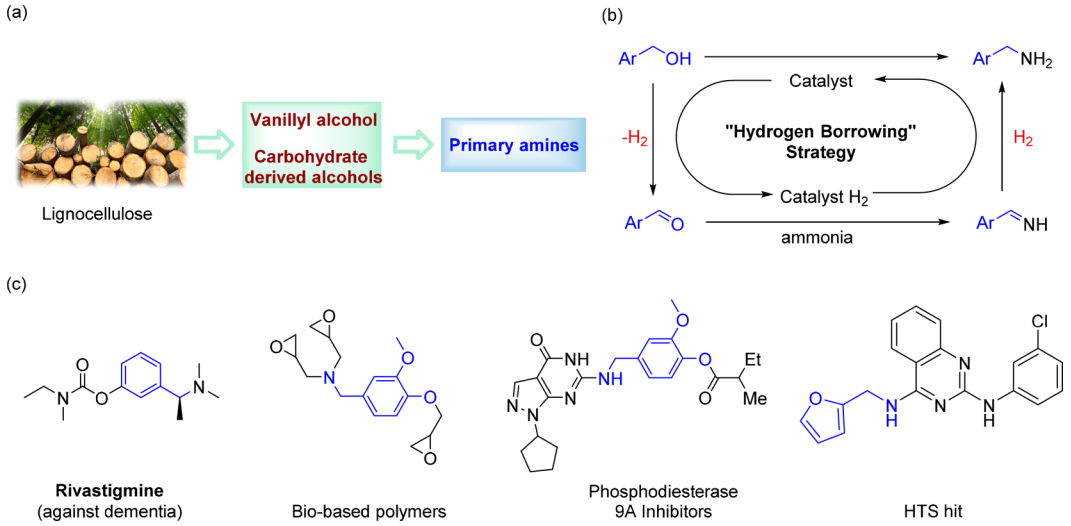
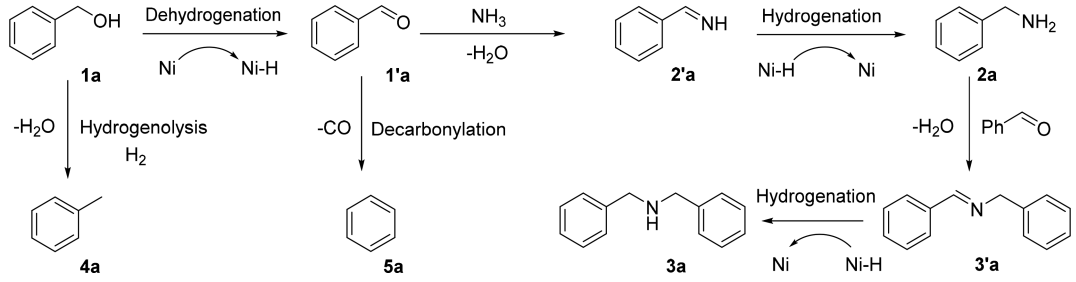


Figure 1. (a) Possible biobased amine building blocks from lignocellulose. (b) General mechanism of the "hydrogen borrowing" strategy. (c) Representative examples of bioactive molecules comprising benzylamine moieties or furfurylamine.

Scheme 1. Possible Reaction Pathways during Direct Amination of Benzyl Alcohol with Ammonia Using Raney Ni As Hydrogen Transfer Catalyst



herein we specifically describe the chemistry of lignin-derived vanillyl alcohol[20] for the first time and demonstrate the challenging conversion of this renewable building block. The product benzylamine can be used, among others, for the production of emerging biobased polymers.[3,4] Our method also allows access to sugar-derived biobased target compounds, such as furfurylamine, 5-methylfurfurylamine, and tetrahydrofurfurylamine as well as aliphatic primary amines. Moreover, we also present sustainable pathways to access *p*-xylylenediamine and *m*-xylylenediamine that are important precursors for the production of thermally stable polyamide fibers such as Kevlar.[21]

EXPERIMENTAL SECTION

Materials. Benzyl alcohol and its derivatives; dodecane; Raney nickel catalysts 2800, 3420, and 4200; $Ni/Al_2O_3–SiO_2$; aqueous ammonia (aq. NH_3, 25 wt %); ammonia in THF (0.4 M); ammonia in dioxane (0.5 M); ammonia carbonate; and all the solvents were purchased from Sigma-Aldrich and used as received. Carbon supported nickel (Ni/C, 10% Ni loading) catalyst was purchased from Riogen, Inc.

Methods. ***Representative Procedures.*** *General Procedure 1.* A 10 mL Swagelok stainless steel microreactor, equipped with a stirring bar, was charged with substrate (1 mmol), 200 mg of catalysts (as specified), 0.4 mL of aq. NH_3 (25%, 5.2 mmol), and 20 μL of dodecane (0.088 mmol) as an internal standard. Then, the reactor was sealed and placed in a preheated aluminum heating block at appropriate temperature (typically 180 °C). After the indicated reaction time (typically 18 h), the microreactor was cooled down to room temperature using an ice–water bath. The crude mixture (a solution) was separated from the metal Ni using a magnet and analyzed by GC-FID directly; conversion and selectivity were calculated based on calibration curves and an internal standard as shown in the Supporting Information, page S3. Then, the product was isolated as HCl salt as described next. The solvent was evaporated under reduced pressure, and diethyl ether (25 mL) was added. After drying over $MgSO_4$, the mixture was filtered and washed with an extra 10 mL of diethyl ether, then 0.5 mL of 1 M HCl in diethyl ether was added. A precipitate was formed immediately; the HCl salt was isolated by filtration and eventually washed with diethyl ether.

General Procedure 2. A 10 mL Swagelok stainless steel microreactor, equipped with a stirring bar, was charged with substrate (vanillyl alcohol, 0.5 mmol), 200 mg of catalysts (as specified), and ammonia carbonate (2 mmol). Then, the reactor was sealed and placed in a preheated aluminum heating block at an appropriate temperature (typically 140 °C). After the indicated reaction time (typically 18 h), the microreactor was cooled down to room temperature using an ice–water bath. The crude mixture was separated from the catalyst by filtration, concentrated *in vacuo*, and analyzed by GC-FID. The residue was purified by flash column chromatography to provide the pure amine product.

Control Reaction and Leaching Test. Control experiments were performed under *general procedure 1* in the absence of catalyst in the Swagelok reactor. The obtained results displayed no formation of any amine product. In order to establish if leached Ni could have contributed to the reaction: two kinds of experiments were conducted, namely, "hot filtration" as well as ICP analysis for both catalytic systems (Raney Ni with aqueous ammonia and $Ni/Al_2O_3–SiO_2$ with ammonium carbonate).[22,23] The results revealed no product formation for both Raney Ni and $Ni/Al_2O_3–SiO_2$ systems (Supporting Information, pages S3 and S4).

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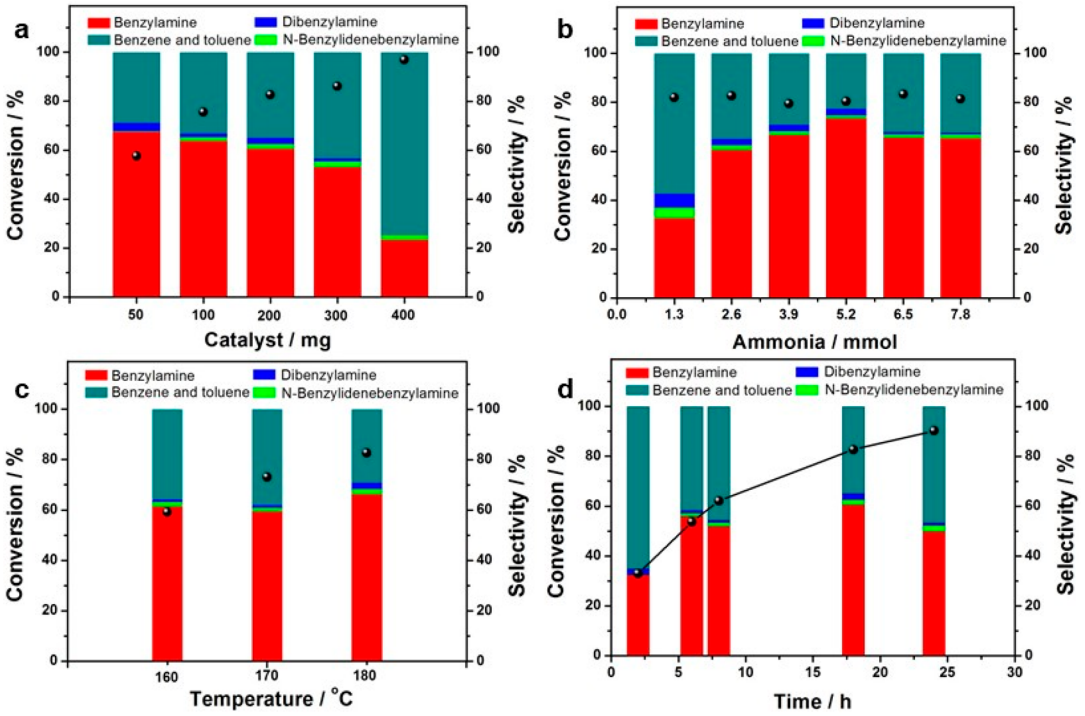

Figure 2. Influence of various reaction parameters on the selectivity of primary benzylamines. Varying amounts of (a) catalyst (50−400 mg), (b) ammonia equivalents (1.3−7.8 mmol), (c) reaction temperatures (160−180 °C, 18 h), and (d) reaction time (180 °C, 2−24 h). General reaction conditions: *general procedure 1*, benzyl alcohol (1 mmol), aq. NH_3 (25 wt %), Raney Ni 2800, and dodecane (internal standard, 20 μL).

RESULTS AND DISCUSSION

With the aim to establish a novel methodology that could be further easily extended to more complex compounds, such as lignin-derived vanillyl alcohol as well as carbohydrate derived alcohols (Figure 1a) for the direct amination of alcohols to primary amines with aqueous ammonia (aq. NH_3) instead of ammonia gas, via the borrowing hydrogen methodology (Figure 1b), we have selected simple benzyl alcohol (**1a**) as a suitable model compound (Scheme 1).

Given the early examples of using Ni catalysts in borrowing hydrogen-based alkylation of amines,[16,17,19] we have evaluated commercially available Ni/C, Ni/Al_2O_3−SiO_2, and Raney Ni catalysts for the primary amine synthesis from benzyl alcohol and aq. NH_3. Using Ni/Al_2O_3−SiO_2 as a catalyst, full conversion was achieved, however only a trace amount of product was observed (Table S1) due to the formation of secondary amine as a major product. Raney Ni (92% conversion and 43% primary amine selectivity) was found more active than Ni/C (36% conversion), therefore we chose Raney Ni for further optimization and evaluated Raney Ni-3020, Raney Ni-4200, and Raney Ni-2800, which all displayed good conversion of 81−88% and varying selectivity values (41−61%). These results are summarized in Figure S1 and Table S2.

Reaction Network. On the basis of the products obtained thus far with Raney Ni (for a typical GC-FID chromatogram, see Figure S2), a reaction network was constructed that is summarized in Scheme 1. The main, desired pathway proceeds through benzyl alcohol (**1a**) dehydrogenation, followed by imine (**2′a**) formation and reduction using the H_2 equivalent "borrowed" from the alcohol. Given the increased nucleophilicity of the primary amine (**2a**) product compared to ammonia, formation of *N*-benzylidenebenzylamine (**3′a**) and the corresponding dibenzylamine (**3a**) is a dominant side reaction. Interestingly, under these reaction conditions, hydrogenolysis of benzyl alcohol to toluene (**4a**) and decarbonylation of the benzaldehyde intermediate to benzene (**5a**) cannot be prevented.

Optimization of the Reaction Conditions. On the basis of the reaction network (Scheme 1), it is clear that restraining the above-mentioned hydrogenolysis and double alkylation side reactions would promote selectivity toward the desired primary amine. Thus, the substrate/catalyst ratio, the nature of the reaction media, reaction time, and ammonia/substrate ratio were investigated, since especially a higher amount of ammonia would favor the formation of primary amine, and in this respect, ammonia solubility in the reaction medium would also play a role. Indeed, solvent screening using Raney Ni-2800 found large dependence of the product selectivity and substrate conversion on the type of solvent used (Table S3). Among the tested solvents, toluene, *t*-amyl alcohol, and *p*-xylene have shown good conversion (over 80%) and selectivity (50−60%) values. Due to the highest selectivity (61%) obtained therein, *p*-xylene, which can also be obtained from renewables, was chosen as an appropriate reaction medium.

After identifying *p*-xylene as a solvent of choice, next the substrate/catalyst ratio, reaction temperature, and reaction time were varied. The optimal amount of catalyst was found to be 200 mg, leading to a good conversion of 83% and selectivity of 61%. With further increasing the catalyst amount, almost full substrate conversion (97%) was achieved, however, hydrogenolysis and decarbonylation side reactions became more pronounced, resulting in benzene and toluene as main products (Figure 2a). Further, it was confirmed that the already used 180 °C is ideal for both conversion and primary amine selectivity than lower temperatures 160−170 °C (Figure 2c). Thus, the product formation profile in the function of reaction time was conducted at 180 °C; this revealed a gradual

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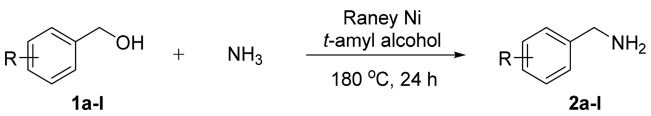
increase in conversion and selectivity from 2 to 18 h reaction time (Figure 2d). The above-mentioned product distributions related to reaction optimization can be found in Tables S4−S7.

From the reaction network (Scheme 1), it is anticipated that a higher ammonia/substrate ratio would increase selectivity to the desired product (**2a**) since conversion of the aldehyde intermediate (**1′a**) to the corresponding imine (**2′a**) needs to compete with aldehyde decarbonylation. Furthermore, providing more ammonia should be beneficial for suppressing double alkylation side reactions as well. Thus, in order to boost selectivity to the desired product, we conducted a series of reactions with varying ammonia amounts (see Figure 2b and Table S5). Gratifyingly, the primary amine selectivity could further be increased to 74% using a 5-fold excess (5.2 mmol) of ammonia compared to the substrate, while still maintaining good conversion levels. Further, the pressure in the minireactor was evaluated by using a Parr reactor of identical volume and was found to be ∼14 bar. A detailed discussion related to this point can be found in the Supporting Information, page S5. Further increasing the amount of aqueous ammonia resulted in a slight drop in selectivity. We consider the water to play an important role in the reaction, which facilitates imine (**2′a**) hydrolysis to the corresponding aldehyde (**1′a**) and , thus, suppresses the formation of the undesired **2′a**.[24] It was also observed that conversion levels consistently remained around 80% independently of the amount of ammonia, as expected. No obvious leaching was detected after reaction by ICP analysis (see Supporting Information page S4 and S5). The Ni content in the solution was 24 ppm, which is comparable with previous literature values.[19]

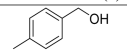
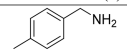
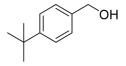
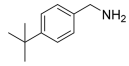
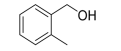
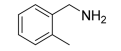
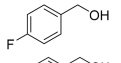
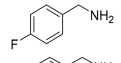
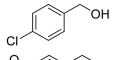
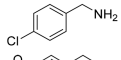
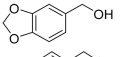
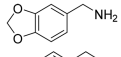
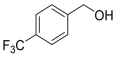
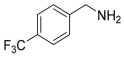
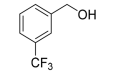
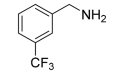
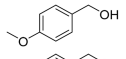
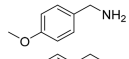
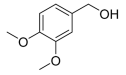
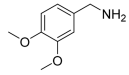
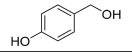
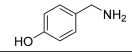
Catalyst Recycling and Reusability. The advantage of using Raney Ni as a catalyst is the ease of reusability due to its magnetic properties. Therefore, we have demonstrated a simple recycling procedure with the help of a magnet. After the first run, the catalyst was washed with the reaction solvent in the microreactor, and subsequently fresh substrate, internal standard, and aq. NH_3 were introduced to carry out the next reaction. With this method, the conversion and selectivity values were roughly maintained for eight cycles. The results are shown in Figure S3, and a detailed products distribution of each run is shown in Table S8. Interestingly, a good conversion of 65−70% and good selectivities of 63−78% were generally obtained. The formation of toluene and benzene side products was highest in the first run, which may be attributed to the small amount of hydrogen present in the catalyst itself.

Primary Benzylamines from Benzyl Alcohols. With the optimized reaction conditions in hand, we next established the scope of the method using benzyl alcohols bearing various electron withdrawing and electron donating substituents. The results are summarized in Table 1, and related experimental data are shown in Figures S8−S15. In general, conversion values and selectivities exceeded those obtained with unsubstituted benzyl alcohol. Benzyl alcohols **1b** and **1c** bearing an electron donating *p*-methyl and *tert*-butyl groups displayed ∼90% conversion and 56% and 70% isolated yields of **2b** and **2c**, respectively (entries 1 and 2). Using an *o*-methyl substituted benzyl alcohol **1d** showed 44% isolated yield of *o*-methylbenzylamine **2d** (entry 3). Good conversion and selectivity were obtained with *p*-fluorobenzyl alcohol **1e** as a substrate (entry 4). However, the *p*-fluorobenzylamine **2e** product was challenging to isolate. Poor results were obtained with the chlorinated substrate **1f** (entry 5) likely due to substrate dehalogenation and catalyst poisoning. Piperonyl

Table 1. Primary Amines via Coupling of Various Alcohols with aq. NH_3[b]



1a-l 2a-l

Entry	Alcohol (**1**)		Product (**2**)		Conv., %[a]	Sel., %[a]
1		**1b**		**2b**	89	72(56)
2		**1c**		**2c**	88	74(70)
3		**1d**		**2d**	59	65(44)
4		**1e**		**2e**	84	62
5		**1f**		**2f**	16	2
6		**1g**		**2g**	91	66(58)
7		**1h**		**2h**	50	90(48)
8		**1i**		**2i**	60	77(50)
9		**1j**		**2j**	90	81(69)
10		**1k**		**2k**	91	74(56)
11		**1l**		**2l**	100	trace

[a]Conversions and selectivities were determined by GC-FID. [b]General reaction conditions, *general procedure 1*: alcohol (1.0 mmol), aq. NH_3 (25 wt %, 0.4 mL), Raney Ni catalyst (200 mg), *t*-amyl alcohol (3 mL), 180 °C, 24 h, isolated yields using ammonia salt method in parentheses.

alcohol **1g** delivered the corresponding pharmaceutically relevant primary amine **2g** in good, 58% isolated yield (entry 6). Substrates bearing both *p*-trifluoromethyl **1h** and *m*-trifluoromethyl **1i** groups displayed around 50% isolated yields of corresponding primary amines (entries 7 and 8).

Moving toward lignin-related building blocks **1j**−**1l** that have not been explored previously, we have found that the 3,4-methoxybenzyl alcohol **1k**, as well as *p*-methoxy substituted benzyl alcohol **1j**, showed excellent conversion (90%) and high selectivity values (entries 9 and 10). Interestingly, when using *p*-hydroxybenzyl alcohol **1l** as a substrate (entry 11), no nitrogen containing products were observed as shown in Figure S4. The main detected products were 4-hydroxytoluene (80%), phenol (17%), and a trace amount of dimer, which could be attributed to known deoxygenative coupling with the formed phenol.[20,25]

Toward Biobased and Other Important Benzylamines. Vanillin is industrially produced from guaiacol by classic "bottom-up" strategies, and the current industrial demand for vanillin is not yet substantial.[26] However, a revived interest in lignin oxidation[27,28] methods applied on both organosolv and Kraft lignin led to an increase of obtainable well-defined building blocks: vanillin and syringaldehyde. As important aromatic platform chemicals, these aromatic monomers will, in the future, serve as starting material for the production of emerging biobased chemicals, polymers, and materials, creating more demand. Many of the target products will contain nitrogen, therefore both reductive

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amination from vanillin as well as the development of novel hydrogen borrowing methods starting directly from vanillin alcohol is of high importance. With a recent focus on lignin depolymerization,[4] both vanillyl and syringyl-alcohol may be, in the future, potentially obtainable directly from lignin or lignocellulose.

Phenolic primary amines are important building blocks for pharmaceuticals[29,30] and polymers[31] (Figure 1c). However, surprisingly, in the literature there is a lack of hydrogen borrowing methodologies applied to vanillyl alcohol, syringyl alcohol, or even the simpler *p*-hydroxybenzyl alcohol as a substrate using ammonia. In line with our ongoing interest in amination chemistry[32,33] and catalytic lignin depolymerization,[34] we sought to develop a new catalytic method for the efficient amination of the valuable biobased alcohols.

In our initial studies, we observed that vanillyl and syringyl alcohols, bearing a free phenol group, behaved markedly different from the structurally related and electronically similar 3,4-dimethoxybenzyl alcohol shown above (Table 1, entry 10). When we used vanillyl alcohols for the amination reaction with Raney Ni and ammonia at 180 °C, the results were similar to those obtained with *p*-hydroxybenzyl alcohol. The main product was 2-methoxy-4-methyl phenol (65%), suggesting that hydrogenolysis of the starting material was prevalent over dehydrogenation. Surprisingly, further decreasing the reaction temperature and screening various ammonia sources have not significantly influenced this tendency, and 2-methoxy-4-methylphenol remained the dominant product in all of the examined reactions. At the same time, due to the lower reaction temperature, also the decarbonylation product *o*-methoxyphenol appeared in significant quantities (Figure 3, Table S9).

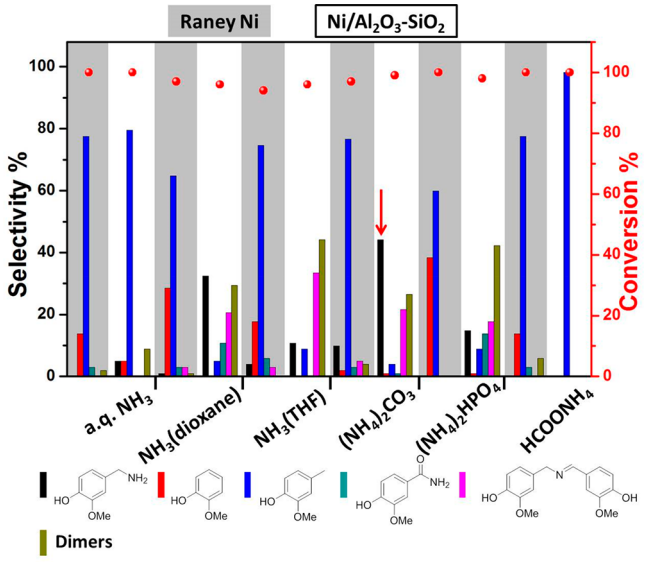

Figure 3. Comparison study between Raney Ni (gray region) and Ni/Al_2O_3−SiO_2(white region) catalyzed vanillyl alcohol amination with various ammonia sources. General reaction conditions: *general procedure 2*, 200 mg of Ni catalyst, 0.5 mmol of substrate, 2 equiv of NH_3 in ammonia salts, 140 °C, 18 h; conversion and selectivity values were calculated by GC-FID. For aq. NH_3: 0.4 mL aq. NH_3, 3 mL *t*-amyl alcohol as solvent. For NH_3 in organic solvents: directly use 3 mL of ammonia in dioxane (0.5 M) or THF (0.4 M) as both solvent and ammonia source.

When examining the product suite obtained during the amination of vanillyl alcohol with ammonia (Figure S5), several differences were observed compared to the reactivity of regular benzyl alcohols, which did not contain a phenol substituent para to the benzyl alcohol moiety. Besides the higher tendency for hydrogenolysis, the formation of dimeric aromatics that did not contain any nitrogen were observed as side products. Indeed, the tendency for vanillyl alcohol to undergo various dimerization pathways (Figure 4), especially

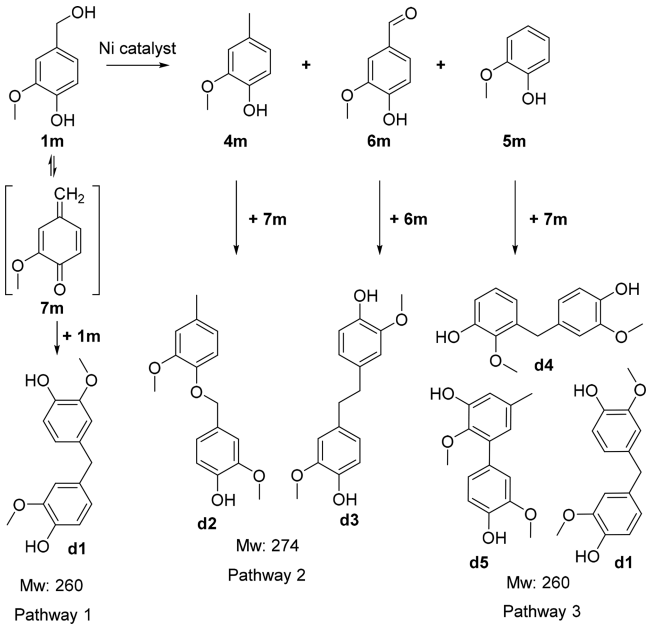

Figure 4. Possible dimerization byproducts detected from amination reaction of vanillyl alcohol.

under basic conditions, involving a quinonemethide intermediate (Figure 4, compound **7m**) is known from early works of Hemmingson and Leary[35] and Dimmel et al.[20] Based on the molecular weight and MS fragments of the byproducts and previous studies,[20,35] herein we propose possible formation pathways of the dimeric byproducts as shown in Figure 4 (a detailed discussion is shown in the Supporting Information, note 4). The ease of water or hydroxide release from these phenolic benzyl alcohols due to resonance stabilization should be the main reason for the prominent side reactions occurring in these substrates, rendering the direct amination that requires maintaining the C−O bond challenging.

Due to the observed prominent hydrogenolysis activity of Raney Ni, we have decided to investigate the use of other Ni-based catalysts. We chose the commercially available Ni/Al_2O_3−SiO_2 catalyst and various ammonia sources for further screening (Figure 3 and Table S10). As before, in all cases, near full conversion was achieved, and $(NH_4)_2CO_3$ emerged as the best ammonia source, with a 45% yield of vanillylamine detected.

Therefore, further optimization was conducted with Ni/Al_2O_3−SiO_2 as a catalyst and $(NH_4)_2CO_3$ as an ammonia source. In particular, the catalyst to substrate and substrate to ammonia ratio was varied as specified in Table 2. It was concluded that a substrate to $(NH_4)_2CO_3$ ratio of 1:4 was optimal for achieving good primary amine selectivities and suppressing over alkylation pathways to a certain extent. For example, excellent conversion (>99%) and good (58%)

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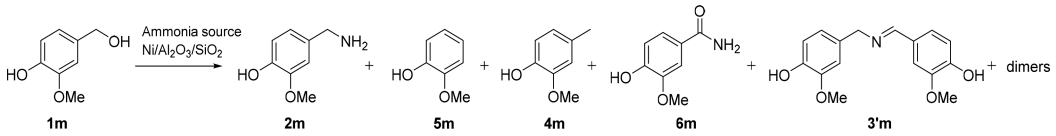
Table 2. Direct Synthesis of Primary Amines from Vanillyl Alcohol and $(NH_4)_2CO_3$ Using $Ni/Al_2O_3–SiO_2$ As a Catalyst[a]



entry	catalyst amount/mg	sub. (mmol)/$(NH_4)_2CO_3$ (mmol) ratio	conversion /%	selectivity/%					
				2m	5m	4m	6m	3′m	dimers
1	100	0.5:1	83	52	2	3	0	19	23
2	100	0.25:1	87	54	0	2	1	25	27
3	100	0.5:2	54	50	1	2	0	23	23
4	200	0.5:2	>99	58 (40)[b]	2	4	0	16	20
5	50	0.5:2	34	56	1	2	0	19	22
6	400	1:4	>99	4	4	55	1	7	29

[a]General reaction conditions: *general procedure 2*, $Ni/Al_2O_3–SiO_2$ catalyst, vanillyl alcohol substrate, $(NH_4)_2CO_3$, 3 mL *t*-amyl alcohol, 140 °C, 18 h; conversion and selectivity were calculated by GC-FID. [b]Isolated yield by column chromatography.

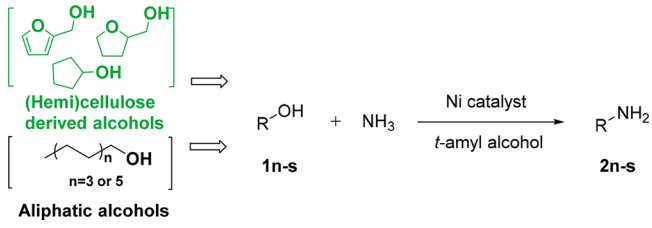
selectivity of vanillylamine with 40% isolated product yield were obtained under specific conditions (Table 2, entry 4). It should be noted that the inherent dimerization pathways could not be suppressed under any of the selected conditions, presenting a general hurdle for achieving higher product selectivity under these conditions, however based on excellent prior work, conversion levels should be improvable in a flow setup.[19] A relatively high, 144 ppm Ni content was detected by ICP analysis, which could be attributed to the existence of the acidic phenol group (see Supporting Information pages S4, S5).

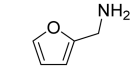
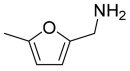
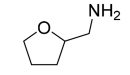
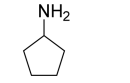
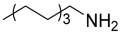
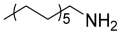
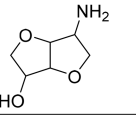
Other Biobased and Aliphatic Alcohols. Further, we applied our catalytic system to other valuable biobased alcohols[36] as well as challenging aliphatic alcohols (Table 3). The results revealed that significantly better yields of furfurylamine (**2n**,52%), 5-methylfurfurylamine (**2o**, 45%), and tetrahydrofurfurylamine (**2p**,41%) were obtained with $Ni/Al_2O_3–SiO_2$ compared to Raney Ni, which could be explained by the presence of hydrogen in Raney Ni favoring the hydrogenolysis of the corresponding alcohol. The aliphatic alcohols, namely cyclopentanol (**1q**), 1-octanol (**1r**), and 1-dodecanol (**1s**), were successfully converted to the corresponding primary amines with 34%, 41%, and 47% isolated yields, respectively. Gratifyingly, when the $Ni/Al_2O_3–SiO_2$ catalytic system was applied to isosorbide, the desired amine **2t** was obtained with 51% yield.

Next, we turned our attention to another class of important benzylamines, *p*-xylylenediamine and *m*-xylylenediamine, that contains important polymer building blocks for the production of thermally stable polyamide fibers such as Kevlar. Industrially, these xylylenediamines are produced by ammoxidizing xylene to phthalonitrile (~400 °C), followed by hydrogenation (100 bar H_2).[37] It is fair to mention that the latter step is highly selective and well-established, however, production of dicyanobenzenes usually requires quite harsh reaction conditions starting from xylene. If, in the future, the production of 1,4- benzenedimethanol becomes feasible from renewables, the direct amination of these alcohols with ammonia (provided selectivity and efficiency improves) will become a superior sustainable method of choice to produce these important diamines. Therefore, proof-of principle methods to accomplish this important direct amination step are highly desired.

To this end, we started our investigation using 1,4-benzenedimethanol (**1u**), aqueous NH_3, and Raney Ni at 180 °C as starting reaction conditions. However, the desired *p*-xylylenediamine (**2u**) was only produced in small quantities (Table 4, entry 1), and besides, full substrate conversion formation of benzylamine (50%) and *p*-methylbenzylamine (32%) was shown as two main products (Table S11). This clearly signified a fast hydrogenolysis under these conditions (180 °C) and an insufficient substrate/ammonia ratio. Indeed, much better *p*-xylylenediamine selectivity was seen when increasing the NH_3 amount. When the reaction temperature further decreased to 170 °C, a good product selectivity was

Table 3. Primary Amines via Coupling of Bio-Based and Aliphatic Alcohols with aq. NH_3[c]



Entry	Product (**2**)		Yield / %	
			Raney Ni	Ni/Al_2O_3-SiO_2
1		**2n**	35	52
2		**2o**	25	45
3		**2p**	26	41
4[a]		**2q**	52(34)[b]	19
5[a]		**2r**	53(41)[b]	38
6[a]		**2s**	55(47)[b]	15
7		**2t**	32	51

[a]Reaction temperature at 180 °C. [b]Isolated yields by ammonia salt method. [c]General reaction conditions: *general procedure 1*, alcohol (0.5 mmol), aq. NH_3 (25 wt %, 0.4 mL), Ni catalyst (200 mg), *t*-amyl alcohol (3 mL), 160 °C, 18 h; yields were determined by GC-FID.

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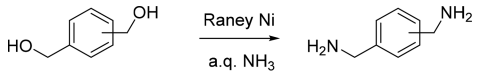
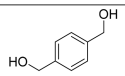
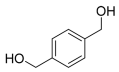
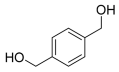
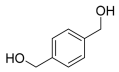
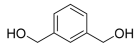
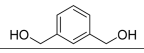
Table 4. Direct Synthesis of Xylylenediamines from Benzenedimethanols and aq. NH_3 Using Raney Ni As a Catalyst[c]



para-: 1u
meta-: 1v
2u
2v

Entry	Substrate	Temperature / °C	a.q. NH_3 / mL	Conversion / %	Selectivity / %
1		180	1.0[a]	>99	8
2		180	2.0	>99	61
3		170	2.0	92	69
4		160	2.0	89	68
5		180[b]	2.0	81	62
6		170[b]	2.0	73	61

[a]3 mL *t*-amyl alcohol and 1 mL aq. NH_3 (25%). [b]0.5 mmol 1,3-benzenedimethanol as substrate; conversion and selectivity values were calculated by GC-FID. [c]General reaction conditions: *general procedure 1*, 200 mg Raney Ni catalyst, 0.5 mmol 1,4-benzenedimethanol substrate, 2 mL aq. NH_3 (25%), 2 mL *t*-amyl alcohol, 18 h.

achieved. Further reducing the reaction temperature to 160 °C resulted in a drop in substrate conversion. When using 1,3-benzenedimethanol as a substrate and the established reaction conditions, *m*-xylylenediamine **2v** was obtained, albeit with slightly lower selectivity (Table 4, entry 5).

CONCLUSION

In summary, we have presented the direct amination of benzyl alcohols with NH_3 for obtaining a range of primary benzylamines, including examples potentially relevant for the pharmaceutical and polymer industry. The method could be extended to direct amination of aromatic diols, to access the important building blocks *p*-xylylenediamine and *m*-xylylenediamine. The conversion of lignin-derived and carbohydrate-derived renewable building blocks as well as challenging aliphatic alcohols was also achieved. To the best of our knowledge, phenolic primary vanillylamine was obtained as the first example of direct amination of vanillyl alcohol with ammonia via the hydrogen borrowing strategy in good yield. With this particular biobased substrate, the $Ni/Al_2O_3–SiO_2/(NH_4)_2CO_3$ catalyst system emerged as the best alternative. The described catalytic methodology is atom-economic and environmentally benign, and it uses commercial Ni catalysts and employs easy-to-handle ammonia sources without the need for the addition of gaseous reagents.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acssuschemeng.9b00619.

Detailed spectrometric, chromatographic, and chemical information and ^1H and ^{13}C NMR spectral data (PDF)

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Notes

The authors declare no competing financial interest.

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